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| EXAMINER | |
|---|---|
| SLOBODYANSKY, ELIZABETH | |
| **ART UNIT** | **PAPER NUMBER** |
| 1652 | 16 |

DATE MAILED: 12/16/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/869,446 | PRZYBYLA ET AL. | |
| | Examin r | Art Unit | |
| | Elizabeth Slobodyansky | 1652 | |

*-- Th MAILING DATE of this communication appears on the cover sheet with the correspondenc address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *25 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *45-114* is/are pending in the application.

4a) Of the above claim(s) *88-111* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *45-87 and 112-114* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. §§ 119 and 120**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6,11,12*.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

## DETAILED ACTION

Claims 45-114 are pending.

### *Election/Restrictions*

Applicant's election with traverse of Group I, claims 45-87 and 112-114, species of the rubredoxin fusion protein with amyloid, in Paper No. 15 filed September 25, 2003 is acknowledged. The traversal is on the ground(s) that "the Examiner has not provided the evidence that the search of all the claims would be seriously burdensome and Applicants therefore traverse the Restriction Requirement" (Response, sentence bridging pages 1 and 2). This is not found persuasive because the Office action mailed July 29, 2003 indicates the reasons because of which the restricted inventions lack special technical features that define the contribution which each claimed invention, considered as a whole, makes over the prior art. Therefore, restriction for examination purposes as indicated in the Office action mailed July 29, 2003 is proper.

The requirement is still deemed proper and is therefore made FINAL.

Claims 88-103 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected Groups II and III, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 15.

Claims 104-111 have been withdrawn previously (Office action mailed July 29, 2003, page 2, last paragraph).

Claims 45-87 and 112-114 are under consideration.

### *Information Disclosure Statement*

The Menon et al. reference has been cited twice, on form PTO-1449 filed June 27, 2001 and on form PTO-1449 filed October 1, 2001. However, the different year (1998 and 1997, respectively) was indicated. The entry on form PTO-1449 filed October 1. 2001 was lined through as representing duplicate. However, the different year (1998 and 1997, respectively) was indicated in two instances. The provided copy does not contain the needed information to determine the correct year. Applicants are required to provide the correct information.

### *Claim Objections*

Claim 112, with dependent claims 113-114, is objected to because of the following: claim 112(a) is directed to non-elected subject matter.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to

> enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 45-51, 53-87 and 112-114 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 45-63, 65-81 and 112-114 are directed to or depend from a polynucleotide comprising a nucleotide sequence encoding a rubredoxin fusion protein comprising an N-terminal rubredoxin constituent and a C-terminal fused polypeptide. Claims 64 and 82-87 are directed to or depend from a polynucleotide comprising a nucleotide sequence encoding a rubredoxin fusion protein comprising an N-terminal rubredoxin constituent and a C-terminal fused β-amyloid.

Claims 46, 48 and 53 recite any proteolytic cleavage site whereas claims 48 and 54 recite any spacer located between rubredoxin and polypeptide. Therefore, the claims are directed to a genus of nucleotides encoding rubredoxin from any source both naturally occurring and man made having any structure. The specification teaches the structure of only a single representative of such species, a rubredoxin from *Desulfovibrio vulgaris* (SEQ ID NO:3). The specification fails to describe any other representative species by any identifying characteristics or properties other than the

functionality of encoding rubredoxin and fails to provide any structure:function correlation present in all members of the claimed genus.

Claims 64 and 82-87 recite nucleotide encoding β-amyloid. Therefore, the claims comprise a genus of nucleotides encoding β-amyloid from any source both naturally occurring and man made having any structure and comprise all allelic and splice variants of a human β-amyloid, for example. The specification teaches the structure of only two representative of such species, fragments of human β-amyloid (page 45; SEQ ID NOs:10, 14). The specification fails to describe any other representative species by any identifying characteristics or properties other than the functionality of encoding β-amyloid and fails to provide any structure:function correlation present in all members of the claimed genus.

Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claim 52 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

It is apparent that plasmid pRUBEX3 is required to practice the claimed invention. The claimed plasmids' sequences are not fully disclosed, nor have all the sequences required for their construction been shown to be publicly known and freely available. As a required element it/they must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If it/they is/are not so obtainable or available, the enablement requirements of 35 U.S.C. § 112, first paragraph, may be satisfied by a deposit of the microorganism(s). See 37 C.F.R. § 1.802.

The specification does not provide a repeatable process for obtaining the microorganism(s) and it is not apparent if the microorganism(s) is/are readily available to the public. The specification must contain the date that the microorganism(s) was/were deposited, the name of the microorganism(s) and the address of where the microorganism(s) was/were deposited.

If the deposit(s) has/have been made under the terms of the Budapest Treaty, then an affidavit or declaration by Applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his/her signature, and registration number, stating that the specific strain(s) has/have been deposited under the Budapest Treaty and that all restrictions imposed by the depositor on the availability to the public of the deposited material will be

irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 C.F.R. § 1.808.

If the deposit(s) has/have not been made under the Budapest Treaty, then in order to certify that the deposit(s) meets the criteria set forth in 37 C.F.R. § 1.801-1.809, Applicant(s) may provide assurance of compliance by an affidavit or declaration, or by a statement by an Attorney of record over his/her signature and registration number, showing that:

(a) during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;

(b) all restrictions upon availability to the public will be irrevocably removed upon granting of the patent;

(c) the deposit(s) will be maintained in a public depository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer;

(d) a viability statement in accordance with the provisions of 37 C.F.R. § 1.807; and

(e) the deposit will be replaced should it become necessary due to inviability, contamination or loss of capability to function in the manner described in the specification.

In addition, the identifying information set forth in 37 C.F.R. § 1.809 (d) should be added to the specification. See 37 C.F.R. § 1.803-1.809 for additional explanation of these requirements.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 48, 64 and 77-79 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 48 recites the limitation "spacer" in line 2. There is insufficient antecedent basis for this limitation in the claim. Claim 48 depends from claim 45 where it appears it should depend from claim 47.

Claim 64 recites "an amyloid peptide or a biologically active fragment, modification or analogue thereof". Biological activity can encompass various activities such as aggregation into fibrils (page 13, lines 12-13), immunogenic, etc. Without knowing the activity, it is impossible to know which fragments are encompassed by the scope of the claim. Modification can be of different type such as chemical or genetic and involve different parts of the molecule. Without defining the modification, it is impossible to determine the metes and bounds of the claim. The term "analogue" is

neither art or specification defined rendering the metes and bounds of the claim unascertainable.

Claims 77 and 78 depend from claim 71(d) wherein claim 71 has steps (a) and (b) only.

Claim 79 is confusing as dependent from claim 71 where it appears it should depend from claim 77.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The date of the Menon et al. reference is taken as October 1997. If the date is October 1998, the rejection is made under 35 U.S.C.102(a).

Claims 45-51, 53-60, 64-71 and 76-81 are rejected under 35 U.S.C. 102(b) as being anticipated by Menon et al.

Menon et al. teach a DNA encoding a 13.6 KD fusion protein comprising a leader protein, a histidine tag sequence, a Factor Xa cleavage site and the 1-40 β-amyloid peptide or 1-42 β-amyloid peptide. Absent the evidence to the contrary, the

leader protein is construed as rubredoxin considering that the construct of the instant invention has the same molecular weight of 13.6 kD and comprises a histidine tag sequence, a Factor Xa cleavage site and either the 1-40 β-amyloid peptide or 1-42 β-amyloid peptide (page 31, lines 17-20). Menon et al. teach the purification of a soluble β-amyloid peptide. Rubredoxin inherently binds $Fe^{2+}$.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 61-63, 72-75, 82-87 and 112-114 are rejected under 35 U.S.C. 103(a) as being unpatentable over Menon et al.

The teachings of Menon et al. are outline above.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use radioactive isotopes for tracking the proteins as required by claims 61-63, 72-75, 82-87 according to their routine use in the art. It would have been further obvious to produce a composition such a vaccine comprising the claimed DNA according to a routine use in the art (claims 112-114).

Claims 45-51, 53-63, 65-87 and 112-114 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ueno et al. (EP 0 781 848A2) in view of Dobeli et al.

Ueno et al. (form PTO-1449 filed June 27, 2001) teach a DNA encoding a fusion protein comprising and N-terminal heat-resistant protein and a C-terminal fused polypeptide (page 2, lines 26-37). Several heat-resistant proteins are mentioned, including *Pyrococcus furiosus* rubredoxin (page 3, lines 6-36, especially line 20). They teach that a heat-resistant protein can be fused directly or indirectly to a DNA encoding a polypeptide (abstract). They teach that linker (spacer) sequence can contain proteolytic cleavage site (page 3, lines 42-52). They teach vectors comprising said fusion proteins and their expression in a host cell with subsequent purification of a polypeptide (page 3, last paragraph; pages 4-12, Examples).

Dobeli et al. (form PTO-1449 filed June 27, 2001) teach a DNA encoding a fusion protein of 133 amino acids comprising a protein tail fused to the N-terminus of either 1-40 β-amyloid peptide or 1-42 β-amyloid peptide. They teach vectors and *E. coli* comprising thereof and production of soluble β-amyloid peptides. They teach that the purification of β-amyloid peptides using NTA column.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the system taught by Ueno et al. for the production of soluble 1-40 β-amyloid peptide or 1-42 β-amyloid peptide. The motivation to produce a β-amyloid peptide is provided by Dobeli et al. who teach the physiological importance

of β-amyloid peptide and difficulties in its recombinant production. One of ordinary skill in the art would have a reasonable expectation of success because Ueno et al. teach that the system is useful with any polypeptide and because Dobeli et al. successfully obtained soluble β-amyloid peptide by expressing it as a fusion protein.

It would have been further obvious to use radioactive isotopes routinely used in the art for tracking the proteins as required by claims 61-63, 72-75, 82-87. It is would have been obvious to visually tracking the protein using inherent ability of rubredoxin to bind $Fe^{2+}$ (claims 49, 55, 60, 67, 78). It would have been further obvious to produce a composition such a vaccine comprising the claimed DNA according to a routine use in the art (claims 112-114).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Elizabeth Slobodyansky whose telephone number is (703) 306-3222. The examiner can normally be reached Monday through Friday from 9:30 AM to 6:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy, can be reached at (703) 308-3804. The FAX phone number for Technology Center 1600 is (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Center receptionist whose telephone number is (703) 308-0196.

E. Slobodyansky

Elizabeth Slobodyansky, PhD
Primary Examiner

December 12, 2003